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Introduction

Overview

The following ten interoperability scenarios have been built by the Clinical Trials Management Systems Interoperability Working Group (CTMSi WG) and analysts during the November ? early December 2008 timeframe. These were built during thrice-a-week, 2-3 hour, conference calls and interim exchanges of e-mail messages, carried out with the intent of brainstorming future capabilities of the caBIG Clinical Trials Suite, including cross-workspace scenarios. This is a work in progress as the team is continuing to identify and build additional scenarios.

One of the main areas of interest for the team is to build interoperability scenarios that cross into the other workspaces -- Imaging, Integrative Cancer Research (ICR) and Tissue Banking and Pathology Tools (TBPT). For instance, two scenarios listed below cross into the Tissue Banking domain.

NOTE: This is a joint collaborative artifact built by Working Group members and analysts.

Clinical Trials Management Systems Interoperability Working Group

The following Working Group members contributed to this effort:

- Vijaya Chadaram, Duke University
- Sharon Elcombe, Mayo Clinic
- Jomol Mathew, Dana Farber Cancer Center

Analysts

The analysts who facilitated the discussions, documented decisions, etc. on this effort include:

- Smita Hastak, ScenPro, Inc.
- Wendy Ver Hoef, ScenPro, Inc.

Guidelines and Assumptions

The team worked under following assumptions while building these scenarios:

1. We should specifically not limit the interoperability scenarios to the current capabilities and functions of the caBIG Clinical Trials Suite of applications.
2. It is appropriate to leverage other efforts at NCI being conducted within the caBIG Clinical Trials Management Systems Workspace.
3. We should look at the complete picture of clinical research as depicted in the Business Architecture Model (BAM) that the Workspace has put together. The current caBIG Clinical Trials Suite is focused on and supports many aspects of the Study Conduct use cases in the BAM. During building of the BAM late last year, Working Group members had identified gaps in tool functionality in terms of developing the Protocol document and initiating a study. The Working Group had identified many high level use cases at that point in both these areas. That work in building BAM has been leveraged here in the first two scenarios.
4. Based on guidance from Workspace leadership, look for natural touch points into the other caBIG Workspaces. We have identified two scenarios with Tissue Banking, and will continue to build more of such cross-domain scenarios.
5. When Workspace leadership chooses the ones to be implemented, we will further flesh out the scenarios and build detailed supporting dynamic artifacts: activity diagrams, sequence diagrams, etc. These analysis artifacts will be detailed enough to allow their implementation by the development teams.
6. The semantics of these scenarios will be harmonized with BAM and the Biomedical Research Integrated Domain Group (BRIDG) model. We have already begun the work of harmonizing with BAM use cases. As the details are fleshed out, the static content of what is being exchanged will be harmonized with BRIDG along with the actors.
7. These scenarios will be vetted by the larger clinical research community (the caBIG Clinical Trials Management Systems Workspace) to validate the scenarios and then updated and extended as needed.
8. These caBIG Clinical Trials Suite interoperability scenarios assume a single site installation of the the caBIG Clinical Trials Suite software - any complications required to support a multi-site installation

will be worked out later with the leadership of the technical teams.

9. All applications and sites using this single site installation use a common subject MRN (locally assigned number).
10. Each Study/Protocol has a unique identifier. The "Coordinating Center Study Identifier" is the unique Study identifier that will be part of the messaging across applications.
11. C3PR is assigning the unique "Study Subject Identifiers" to all study subjects (system-assigned number)
12. Other assumptions TBD.

CTMS Interoperability Scenarios - DRAFT

NOTE: These interoperability scenarios are in a draft stage. When a scenario is selected for development, the storyboards may be revised as the actual process flow is worked out based on input from the tech teams. The vetting of these scenarios with the caBIG Clinical Trials Management Systems Workspace may also result in updates to the scenarios.

Scenario #1: Protocol Authoring

Preface: This scenario envisions a new protocol authoring and management tool for functionality that is not currently available in any of the CCTS applications. This tool would include the functionality described in the first and second storyboards as well as potentially others. The tool would not only capture protocol representation but also change control and versioning to accommodate initial development and later amendments and their review processes. Furthermore, it would provide for computable protocol representation that would be utilized by all the other CTMS Suite applications. Amendments could be supported in the same way, but an extension to this interoperability scenario will be developed to address that situation ? thus the scope of this scenario is just the initial development of a protocol, not amendments to an existing protocol.

Storyboard: A Lead Investigator is ready to develop a new protocol and its associated materials from a concept that has been approved for drug X for a phase III breast cancer trial. The Study Protocol Coordinator reviews the concept (assuming concept is approved) and logs into a computerized tool for assisting her in drafting the protocol document and associated materials (refer to BAM for the list of associated materials) and generating study meta-data. She enters the protocol information and associated metadata into appropriate templates in a computable manner, all of which will later be used to generate the documents as well as initiate study conduct-related systems. In addition to the Study Protocol Coordinator, other study team members or other specialists are involved in authoring various sections of the protocol and its associated materials for their specialty areas (for example, safety coordinator, quality control specialist, etc.). The Study Protocol Coordinator generates the protocol document and associated materials automatically from the entered information on an as needed basis. When the first draft of the protocol and associated materials are ready for review, the Study Protocol Coordinator changes the status of the protocol accordingly. This is a touch point to the Protocol Review Tracking Process storyboard.

The Study Protocol Coordinator shepherds the protocol through the review process (per the storyboard below) and when the Protocol is ready to be activated, the computable protocol representations can be consumed or utilized by the other CTMS Suite applications, i.e. C3PR, PSC, LabViewer, caAERS and CDMS and any

other applications involved in clinical research, for example, caTISSUE. The Study Protocol Coordinator, using the Protocol Authoring and Management tool, initiates a message to the other applications, notifying them that the new protocol is ready for consumption (amendments could be a variation on this storyboard). Later, a clinical research staff member goes into the applications, sees the notifications, and initiates a request to the Protocol Authoring and Management tool for detailed study data appropriate for each application.

Alternate Path: As the protocol and associated materials go through the review process, to incorporate the reviewer's comments, protocol authoring continues until the final draft is generated. The Study Protocol Coordinator versions the protocol and associated materials to correspond with the review cycles.

Activity Diagram: Scenario #1 - Protocol Authoring

BAM Actors

- **Lead Investigator**: This individual provides guidance for and has responsibility for the overall study conduct and oversees multiple investigators at multiple sites. NOTE: In a single site trial, this role is synonymous to a Principal Investigator and in some multi-site studies this is called a Study Chair. ICH E6 refers to this as a "Coordinating Investigator".
- **Coordinating Center Protocol Coordinator**: Supports the study team (e.g. lead investigator who has overall responsibility, plus biostatistician, management personnel, etc.) in ensuring all components of the detailed research plan are completed and continues to coordinate all those activities throughout the protocol life cycle.

BAM Touch Points

- Plan Study > Develop Protocol and Associated Materials and sub use cases
- Plan Study > Amend Protocol and Associated Materials
- Enterprise Common Resources > Manage Protocol ? need to coordinate/reconcile/harmonize overlap between protocol management in Plan Study vs Enterprise Common Resources
- Enterprise Common Resources > Manage Organization
- Enterprise Common Resources > Manage Person

Scenario #2: Protocol Review Tracking - Study-Level Perspective

Preface: This storyboard is an extension to the protocol authoring storyboard to enable the participation of internal and external reviewers who in reality actually participate in the authoring of the protocol by providing comments, content, etc. For example, the pharmacist may write the drug information section, the nurse might write the drug administration information in terms of supportive care, or the external sponsor, such as DCP or CTEP, would provide comments on the adverse event reporting rules included in the protocol. Amendments could be supported in the same way, but an extension to this interoperability scenario will be developed to address that situation ? thus the scope of this scenario is just the initial development of a protocol, not amendments to an existing protocol. Protocol review and tracking occurs at multiple places (study-level and site-level), but this storyboard is only focused on the study-level perspective.

Storyboard: Once the first draft of the protocol has been generated, the Study Principal Investigator or Study Protocol Coordinator initiates the review process. Part of the review process, for some reviewers, may actually

be contributing to the content of the document. The Study Protocol Coordinator identifies a list of required internal and external entities whose review and/or approval are required prior to study activation. This information includes the review sequence, dependencies between reviews and the organization or individual who will perform each review based on protocol-specific needs. The Study Protocol Coordinator enters the information into the Protocol Authoring and Management tool which supports managing the review process. The support tool provides the review status to enable the management of the process.

The protocol document and its associated materials are made available to the appropriate review entity(s) for review and comments and/or approval. The internal reviewers perform their review within the Protocol Authoring and Management tool which also captures their comments and proposed document changes. The external reviewers' comments are stored in the tool and evaluated by the study team. Only authorized personnel can modify the computable representation of the protocol and its associated materials. This is a touch point to the Protocol Authoring storyboard.

After all reviews are performed and all required approvals are obtained, the protocol is activated by the Coordinating Center.

Notes:

- The reviewers may include the study team, peer reviewers, internal committees, organ site chair, study committee chair, and other designated reviewers; and the individuals may cross institutional boundaries such as for cooperative groups, international studies, etc. while still being part of an organization.
- It would be ideal to have a collaborative tool that could support and track this internal process and would provide:

    1. the ability to capture comments from other tools into the single tool;
    2. multiple ways of viewing the comments, including looking at the document and seeing what the comments are inline, or simply having a summary of all comments on a given protocol;
    3. the ability to bounce back and forth between protocol authoring and review process functions;
    4. privileges to protect documents so only authorized people can see and/or update the documents and changes.
- DocuMart provides some of this functionality from the CTEP perspective and could be reviewed for possible integration.
- This same process could be used for protocol amendments as well.

Activity Diagram: Protocol Review Management - Study-Level Perspective

BAM Actors

- **Lead Investigator**: This individual provides guidance for and has responsibility for the overall study conduct and oversees multiple investigators at multiple sites. NOTE: In a single site trial, this role is synonymous to a Principal Investigator and in some multi-site studies this is called a Study Chair. ICH E6 refers to this as a "Coordinating Investigator".
- **Coordinating Center Protocol Coordinator**: Supports the study team (e.g. lead investigator who has overall responsibility, plus biostatistician, management personnel, etc.) in ensuring all components of the detailed research plan are completed and continues to coordinate all those activities throughout the protocol life cycle.
- **Reviewer Actors are TBD**

BAM Touch Points

- Plan Study > Review Protocol and Associated Materials (wiki) => suggested name change: Manage Protocol Reviews; depending on the type of protocol some of these reviews may or may not occur:
    - ♦Placeholder: Perform Scientific Review
    - ♦Placeholder: Perform Logistical Review
    - ♦Placeholder: Perform Peer Review
    - ♦Placeholder: Perform Statistical Review
- Plan Study > Amend Protocol and Associated Materials
- Plan Study > Perform Final Review and Approve Protocol (EA file)

Scenario #3: Automated Adverse Event Grading Based on Laboratory Data

Pre-conditions:

1. LabViewer has metadata about which studies use which lab tests - this may not end up being a pre-condition if therer are other ways of architecting a solution.
2. LabViewer has metadata about which studies use which assessment methods (e.g. CTCAEV3 or CTCAEV4, etc)

Storyboard: A Clinical Research Associate (CRA) selects a subject for a given time period in the research center LabViewer and indicates that she wants only out-of-range lab values. The LabViewer retrieves all the out of range lab values (distinct labs, regardless of study) and submits them to the automated Adverse Event (AE) grading application (CALAEGS). The LabViewer then displays all the out-of-range lab values with their automatically assigned AE grades and provides a link for CRA to select a grade when a qualitative assessment is required to determine the grade or when the CRA needs to select which grade applies based on other criteria. The CRA reviews and validates the grades for each lab value and selects labs to send as AEs to the AE reporting system (caAERS). The system prompts the CRA to select the study to send as context information to caAERS if the subject is on more than one study. Then LabViewer exports those lab values and associated grades to caAERS. Upon completion of additional AE information data entry in caAERS by the CRA, caAERS will determine which AEs need to be loaded to the Clinical Data Management System (CDMS, protocol-specific, not all AEs are collected for every study). caAERS will also assess the AEs for expedited reporting requirements and institution-specific reporting requirements and, if required, will initiate the reporting process. The CRA interacts with caAERS to provide additional AE information to be included in the reports and to submit to AdEERS, MedWatch or regulatory reporting recipient.

Notes:

- Consider CALAEGS (City of Hope) as automated AE grading application.

Activity Diagram: Automated Adverse Event Grading Based on Laboratory Data

BAM Actor

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the

Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Related use case: Placeholder: Conduct Study > Manage Subjects > Initiate and Maintain Subject-Specific Study Calendar > Order Subject-Specific Study Activities (in the clinical system) ? should we break these out into several different categories?
- Related use case: Redefine: Conduct Study > Manage Subjects > Initiate and Maintain Subject-Specific Study Calendar ? definition doesn?t cover maintaining schedule though storyboard for use case does
- Related Placeholder: Conduct Study > Manage Subjects > Manage Study Subject Activities > Administer Clinical Protocol Activities > Collect Clinical Specimens
- Conduct Study > Manage Subjects > Collect Data - working groups are breaking this down into specific data collection use cases, need to review which of those belong here
- Conduct Study > Manage Subjects > Identify AE
- Report & Analyze Study > Coordinating Center and Participating Site > Generate Safety and Regulatory Reports.

NOTE: Review expedited AE Reporting use cases developed by the Reporting and Sharing SIG.

Scenario #4: Load Study-Specific Subset of All Laboratory Values for a Subject into Clinical Data Management System

Assumptions:

1. These CCTS interoperability scenarios assume a single site installation of the CCTS software - any complications required to support a multi-site installation will be worked out later with the leadership of the technical teams.
2. All applications and sites using this single site installation use a common subject MRN (locally assigned number).
3. Each Study/Protocol has a unique identifier. The "Coordinating Center Study Identifier" is the unique Study identifier that will be part of the messaging across applications.
4. Some clinical lab data system is able to push or send the lab results to LabViewer.
5. This use case could extend the protocol authoring use case above if it enables metadata about the protocol to be captured in computable form. If there is no protocol authoring scenario, the capability of capturing a list of study-specific labs would have to be added to the LabViewer as supplemental study data.

Pre-Conditions:

1. LabViewer already has the study information.
2. LabViewer has access to a list of study-specific labs either via the protocol authoriing tool or all of the study-specific labs are identified as supplemental study metadata in LabViewer.

3. Study subject is already registered on the study.
4. Lab results have already been loaded in the LabViewer.

Storyboard: The Clinical Research Associate (CRA) opens caXchange LabViewer and specifies a subject, a study, a time period and asks for study-specific laboratory values (rather than all labs for that subject during that time period). Results for all protocol-specific labs are displayed in LabViewer - this filtering capability makes it easier to identify which ones need to be loaded to the Clinical Data Management System (CDMS; note that this is an enhancement to an existing use case). This reduces the number of labs that need to be reviewed by the CRA. (There are not likely to be many subjects that have labs beyond what the protocol calls for, but those subjects may have lots of data.) The CRA marks the lab values to be loaded to the CDMS and executes the send function.

Note: This storyboard is applicable if the study requires collecting lab values on case report forms (e.g., via a CDMS). This would also enable Patient Study Calendar (PSC) to be configured, i.e. if we know what labs are associated with the study.

Post-Conditions:

1. Selected lab results loaded to CDMS.
2. Confirmation message from CDMS is received by LabViewer.

Activity Diagram: Load Study-Specific Subset of All Laboratory Values for a Subject into Clinical Data Management System

BAM Actors

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Related due to pre-condition: Plan Study > Develop Protocol and Associated Materials
- Related Placeholder: Conduct Study > Manage Subjects > Manage Study Subject Activities > Administer Clinical Protocol Activities > Collect Clinical Specimens
- Conduct Study > Manage Subjects > Collect Data - working groups are breaking this down into specific data collection use cases, need to review which of those belong here
- Placeholder: Conduct Study > Manage Subjects > Manage Study Subject Activities > Administer Clinical Protocol Activities > Collect Laboratory Values ("collect" includes getting data from clinical record into CRF/research system/CDMS)

Scenario #5: Post-(Study)Registration Specimen Collection (PSC and caTissue)

Preface: Protocols have a defined list of time points when biospecimens will be collected on a periodic basis for subjects on that study. This study calendar, even when made subject-specific in PSC, is still only a plan - it doesn't mean that the activities have been scheduled in the clinic yet. Those activities typically are scheduled one or two at a time for the next set of appointments rather than all future appointments.

Pre-Conditions:

1. Protocol metadata has already been provided to caTissue by the Protocol Authoring tool (see scenario #1).
2. The biospecimen-related activities have been part of the metadata captured during protocol authoring, so that PSC templates can be initialized.
3. The PSC template has already been created for the study in this scenario.
4. This study has been configured in C3PR to include the caTissue (specimen collection) protocols associated with it.

Assumptions:

1. All activities in PSC (and possibly also in the Protocol Authoring tool's study activity metatdata) have the ability to be typed based on typical categories that may be used by other applications.
2. The entire CTMS Suite of applications and caTissue are all installed and configured to interact with each other.

Storyboard: When a subject is registered to a study, a subject-specific study calendar is created in a study calendaring system, e.g. Patient Study Calendar (PSC). All the activities planned for this subject on the study will be displayed to the Clinical Research Associate (CRA). The CRA reviews and validates this information in PSC and activates the study calendar. The activation process automatically initiates a process to notify a biospecimen tracking system (e.g., caTissue) to enable that application to create a biospecimen collection calendar. Updates to the subject schedule for biospecimen-related activities (type = biospecimen-related) trigger a similar update to the biospecimen collection application. For instance, when a given biospecimen collection activity is scheduled, if the scheduled date is different than the original planned calendar date, the CRA logs into PSC, updates the calendar date with the scheduled date and saves the change. This change automatically triggers an update message containing the new scheduled date to be sent to caTissue. caTissue receives the update and saves the change in its subject-specific biospecimen collection calendar.

Alternate Interoperability/Integration: Due to overlaps between Protocol Registration (from Enterprise Common Resources (ECR)), patient information (in Cancer Center Participant Registry (C3PR)) and calendaring (in Patient Study Calendar (PSC)), organization and investigator (person) information (ECR), we should evaluate the data common to these systems on a larger scale. For example, should caTissue utilize the calendaring features of PSC rather than its own calendaring? (PSC may be more robust.)

Note: This could be applied to an Imaging platform (NCIA), gene expression tool (caArray), and any other assay-based system as well.

Activity Diagram: Post-(Study)Registration Specimen Tracking

BAM Actors

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Related due to preface: Plan Study > Develop Protocol and Associated Materials
- Conduct Study > Manage Subjects > Manage Subject Study Registration (and sub use cases)
- Conduct Study > Manage Subjects > Initiate and Maintain Subject-Specific Study Calendar
- Conduct Study > Manage Subject > Manage Subject Schedule
- Conduct Study > Manage Subjects > Collect Biospecimens
- We assume that there are caTissue use cases that are touch points here as well (whether or not they have a formal BAM).

Scenario #6: Pre-Registration Specimen Collection and Tracking (C3PR and caTissue)

Preface: When a subject is being considered for study registration for which a central pathology review is required to determine eligibility (or any other protocol-specific central review requirement), the biospecimen processing lab should be informed.

Pre-Conditions:

1. The investigators have received all the regulatory approvals, such as 1572, financial disclosure, etc.
2. The study has received all the regulatory approvals for the site(s), including IRB approval.
3. The study is approved and open for accrual at the site.
4. The study requires a specific test or analysis to determine eligibility and/or treatment.
5. The subject has signed the consent agreeing to provide the biospecimen.

Storyboard: The Clinical Research Associate (CRA) pre-registers the patient in the registration system (C3PR) at which point they receive a unique identification number. Pre-registration triggers a message to the specimen tracking system (caTissue) to notify it that a specimen is coming. caTissue receives the message and automatically initiates a specimen record with status "expected". Meanwhile, the specimen is collected and labeled by the Clinical Staff, and sent in a protocol-specific kit to a Central Performing Laboratory which is using caTissue. The Central Performing Laboratory personnel await the arrival of the specimen, process it when it arrives and send the results to the CRA. Once the subject is determined to be eligible, the CRA registers the subject on the study.

Post-Conditions:

1. Pre-registration completed successfully.
2. Study Subject Notification and Specimen Alert received by caTissue.
3. Specimen processed.

4. Test results received by CRA.
5. Test result values stored as part of eligibility checklist by C3PR.
6. Study subject registration is either...

    1. completed or
    2. canceled.

Activity Diagram: Pre-Registration Specimen Collection and Tracking

BAM Actors

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected. NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.
- **Clinical Staff**: Any clinical or research individual responsible for collecting the specimen.
- **Central Processing Lab Personnel**: Lab technicians or Pathologists. (This could be a Tissue Banking and Pathology Tools (TBPT) Workspace role.)
- **Lead Investigator**: This individual provides guidance for and has responsibility for the overall study conduct and oversees multiple investigators at multiple sites. NOTE: In a single site trial, this role is synonymous to a Principal Investigator and in some multi-site studies this is called a Study Chair. ICH E6 refers to this as a "Coordinating Investigator".

BAM Touch Points

- Conduct Study > Manage Subject > Manage Subject Study Registration (and sub use cases)
- Conduct Study > Manage Study at Coordinating Center > Register Subjects
- Conduct Study > Manage Subject > Manage Study Subject Activities > Administer Clinical Protocol Activities > Collect Biospecimens
- Conduct Study > Manage Subject > Initiate and Maintain Subject-Specific Study Calendar
- Conduct Study > Manage Subject > Manage Subject Schedule
- Recommend working group consider pre-registration as part of Manage Subject Study Registration or more likely Screen for Eligibility. Based on how the protocol is written, some protocols have you pre-register before screening (phase 1 reservations, central pathology review), others screen first then register (no pre-registration); however pre-registration is not always done for determining eligibility but for other reasons (e.g. determining study treatment). Consider adding a Perform Pre-Registration Centralized Lab Evaluation or something similar as a use case optionally related to Screen for Eligibility.

Scenario #7: Get Report from Electronic Medical/Health Record to Clinical Data Management System (CDMS and EMR/EHR)

Preface: Pathology Reports, Operative Reports, Imaging Reports at present exist only in the Hospital Electronic Medical Records (EMR) systems. Moving selected study-related reports into a Clinical Data Management System (CDMS) will facilitate researchers' access to this data.

Storyboard: A Clinical Research Associate (CRA) accesses the CDMS application to search for a subject and enter clinical data. She selects the subject and then the appropriate Case Report Form (CRF); for example, she may select the "Surgical History" Form. The data required to complete this CRF can only be found in the Operative Report (almost always unstructured data, like a clinical note) which is typically available in the Hospital's EMR/EHR system. The staff member requests the CDMS to retrieve a specific Operative Report based on subject id and the dates associated around it. She reviews the Operative Report and saves it in the CDMS with Personal Health Information (PHI) removed. Based on the information in this Operative Report, she completes the Surgical History CRF.

Note: This would allow the CRA to save the source document with the CRF in an electronic fashion. At present most cancer centers save hard copies of the Operative Report at the cancer center in patient binders for auditing purposes. Implementation of this use case will need to address 21 CFR compliance issues. This will be a very useful scenario for multi-site trials. At present, in multi-site trials, the participating sites fax the Operative Report to the Coordinating Center so that the Coordinating Center has this information to put into their binders. Some cancer centers may scan these Operative Reports.

Activity Diagram: Get Report from Electronic Medical Record/Electronic Health Record to Clinical Data Management System

BAM Actor

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Conduct Study > Manage Subject > Collect Data - working groups are breaking this down into specific data collection use cases, need to review which of those belong here
- Placeholder: Conduct Study > Perform Study Quality Control > Perform Subject-Specific Quality Control, with sub-use cases:
    - ♦ Verify Eligibility
    - ♦ Confirm Response to Treatment
    - ♦ Validate Treatment Dosing/Timing
    - ♦ Evaluate Toxicity
    - ♦ Each of these could optionally include another use case called Review CRFs and Copies of Source Documents for Discrepancies/Concurrence

Scenario #8: Management of Routine Non-Laboratory-Based Adverse Events (caAERS and CDMS)

Assumptions:

1. Protocol metadata includes which AEs must be recorded in CDMS and which AEs must be reporting to various targets.
2. For main storyboard: caAERS rules engine has been configured based on the protocol metadata for how to determine which AEs must be recorded in the CDMS and which AEs must be reported to regulatory agencies.
3. For alternate path: New CDMS (if procured) is configurable/extended and has been configured to be able to collect AE data and send it to caAERs without performing the recordation of the data.
4. Both the main storyboard and the alternate path are assumed to be executed in real time rather than interactions managed by batch jobs.

Storyboard: A Clinical Research Associate (CRA) enters non-lab Adverse Events (i.e., reports of adverse events not based on laboratory data) into caAERS for a subject on a clinical trial. Upon completion of Adverse Event (AE) information data entry in caAERS, caAERS determines two things:

1. which AEs need to be loaded to the Clinical Data Management System (CDMS; this determination is protocol-specific).
2. which AEs need to be reported in an expedited manner.

For those AEs where the rules engine determines that they are to be loaded to the CDMS, caAERS sends the AE information to CDMS which then records the data. For those AEs where the rules engine determines that loading to CDMS is not required, the CRA may override and force the load to CDMS. For those AEs where the rules engine determines that they are to be reported in an expedited manner, caAERS prompts the CRA to enter additional AE information, records the information, sends the report(s) to the appropriate authorities and sends a notification to CDMS that a report was sent.

Alternate Path: (path elements are in yellow in activity diagram) The alternate path provides for initiating this process from the CDMS data entry. AEs are entered directly into the CDMS and then sent to caAERS. The worklfow then continues the same as above. We welcome workspace feedback on this alternate path.

Activity Diagram: Management of Routine Non-Laboratory-Based Adverse Events

BAM Actor

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Conduct Study > Manage Subjects > Collect Data - working groups are breaking this down into specific data collection use cases, need to review which of those belong here

- Conduct Study > Manage Subjects > Manage Study Subject Activities > Evaluate Study Subject Status > Identify AE
- Report & Analyze Study > Coordinating Center and Participating Site > Generate Safety and Regulatory Reports

Scenario #9: Automated Matching of Patients to Trials Based on Eligibility Criteria

Preface: This has a dependency either on the Protocol Authoring interoperability scenario being supported or another means of providing a computable representation of eligibility criteria.

Assumptions:

1. The National Cancer Clinical Trials Database (CTRP Extended) contains a computable representation of the eligibility criteria for the protocol, a synopsis of the protocol, and the sites where the study is being executed.
2. The patient, family member or physician has access to health/diagnosis information needed for eligibility determination.

Storyboard: Once a patient receives a diagnosis of cancer, the patient, family member or the physician decides to identify clinical trials for which the patient may be eligible. The patient or physician initiates a centrally located clinical trials matching application. The system prompts the user to enter the disease site and type. The user enters the disease site and type and the system then tailors the rest of the process accordingly. The system prompts for disease-specific information such as lab data, markers, histology, disease stage, performance status, etc. (TBD by project analysis), the user enters that information and any filtering criteria requested by the application such as distance, institution (i.e. dropdown with name and CTEP code), etc. (TBD by project analysis), and searches for possible matches. The matching application sends the eligibility and filtering criteria to the National Cancer Clinical Trials Database (CTRP Extended) which performs the match and returns the results to the matching application. The application displays all studies that match (approximately 80% match) the provided criteria along with the sites/locations where the study is open and the contact information.

Notes:

- The challenge is to define a coding scheme for all kinds of eligibility data (structured, computable representation) - this will require a significant amount of analysis. The goal would be to determine an 80% chance of eligibility.
- Refer to Clinical Research Filtered Query (CRFQ)- SFS by Charlie Mead, documenting the "how" of how this could be done algorithmically.
- This scenario may be considered outside the current scope of the caBIG Clinical Trials Suite, i.e., depending on whether CTRP can interface with the Suite and be extended to include a matching service/module.
- A related scenario might be the need for potential trials to search for local candidate patients (has to be platform agnostic, might work well for data repositories ? could be searched for tumor specific registries/warehouses, would require IRB approval for that). This may work for retrospective research as well as prospective research. This is a potential touch point with the Population Sciences Special

Interest Group. This scenario is not developed in this round.
- caMATCH, and its successor, BCTNation, has some of this functionality.

Activity Diagram: Automated Matching of Patients to Trials Based on Eligibility Criteria

BAM Actor

- **Physician**: The physician providing the standard of care. (New actor to BAM)

BAM Touch Points

- Related due to preface: Plan Study > Develop Protocol and Associated Materials
- Conduct Study > Manage Subject > Screen for Eligibility
- Placeholder: Conduct Clinical Practice Activities (outside scope of Clinical Research, but may be related to a study, could be Population Sciences-related as well), with sub-use cases:

    - ♦ Collect Medical Records for Diagnostic and Physical Status Information
    - ♦ Identify Possible Study Matches

Scenario #10: Study Calendar Entered in Patient Study Calendar and Interfacing with Clinical Data Management System

Storyboard: After completion of a scheduled visit for a study subject, the Subject Study Calendar Manager updates the calendar in the Patient Study Calendar system (PSC) with the actual visit date and sets the status appropriately. PSC sends a notification to the Clinical Data Management System (CDMS) to alert the latter that the scheduled visit is completed; the CDMS then generates an alert to the Clinical Research Associate (CRA), at next login, to complete the appropriate visit-specific Case Report Forms (CRFs). For example, a patient completes an office visit and the calendar is updated in PSC, triggering a reminder to the CRA to fill out the physical exam form in the CDMS. The same kind of interoperability alert to CDMS is used for all the subject visits in PSC.

Note: This is not currently regarded as a high-priority use case. This could be used as a stand-alone feature.

Activity Diagram: Study Calendar Entered in Patient Study Calendar and Interfacing with Clinical Data Management System

BAM Actor

- **Clinical Research Associate (CRA)**: This individual is responsible for operationalizing the study subject specific activities in the clinic including ensuring that the subject is managed according to the Protocol and the appropriate data are collected.

NOTE: This role may be defined at a very high level in BAM and will need to be reviewed to decompose further down based on functionality.

BAM Touch Points

- Conduct Study > Manage Subject > Manage Study Subject Activities > Manage Study Subject Schedule > Initiate Study Subject-Specific Study Calendar
- Conduct Study > Manage Subject > Manage Study Subject Activities > Manage Study Subject Schedule > Maintain Study Subject-Specific Study Calendar
- Conduct Study > Manage Subject > Manage Study Subject Activities > Manage Study Subject Schedule > Manage Study Subject Activities in Clinical Scheduling System
- Conduct Study > Manage Subject > Collect Data - working groups are breaking this down into specific data collection use cases, need to review which of those belong here

Submit Feedback

Please submit feedback, comments, and questions about the Interoperability Scenarios through the Clinical Trials Management Systems (CTMS) General discussions forum. Please reference the Storyboard number in your feedback.

- CTMS Interoperability Scenario Feedback